

Claim 1. (currently amended) A method for identifying neoplasias responsive to treatment with compounds that selectively inhibit neoplasia, comprising ~~exposing a sample of the neoplasia to a compound that has cGMP-specific PDE inhibition activity and determining whether the compound inhibits the neoplasia.~~ (a) removing a sample of neoplastic tissue from a patient, (b) growing cells from the sample as explants in vitro, (c) contacting a sample of said cells with a compound that has cGMP-specific PDE inhibition activity, (d) comparing the growth of the cells in the presence of the compound with the growth of cells in the absence of the compound, and (e) determining whether the growth of the neoplasia is sensitive to inhibition by the compound.

Claim 2. (cancelled)

Claim 3. (cancelled)

Claim 4. (original): A method for identifying neoplasias responsive to treatment with a cGMP-specific PDE inhibitor comprising determining the level of cGMP-specific PDEs in a sample of neoplastic tissue, wherein an elevated level of cGMP-specific PDEs in the neoplastic tissue, relative to normal tissue, is indicative that the neoplasia has potential for being treated by a cGMP-specific PDE inhibitor.

Claim 5. (original): The method of claim 4 wherein the determination of the level of cGMP-specific PDEs in the neoplastic tissue comprises determining the amount of cGMP-specific PDE protein in the neoplastic tissue sample.

Claim 6. (original): The method of claim 4 wherein the determination of the level of cGMP-specific PDEs in the neoplastic tissue comprises determining the amount of mRNA encoding for GMP-specific PDEs in the neoplastic tissue sample.

Claim 7. (original): The method of claim 4 wherein the determination of the level of cGMP-specific PDEs in the neoplastic tissue comprises determining the cGMP

hydrolytic activity of GMP-specific PDEs in the neoplastic tissue sample.

Claim 8. (withdrawn): A method for identifying neoplasias from a patient responsive to treatment with a cGMP-specific PDE inhibitor comprising the steps of:

- a) obtaining a suspected neoplastic tissue sample from the patient;
- b) contacting the sample with an antibody that is immunoreactive with cGMP-specific PDEs under conditions effective to allow the formation of immune complexes; and
- c) detecting the complexes thus formed,

wherein an elevated amount of cGMP-specific PDEs in the neoplastic tissue, relative to normal tissue, is indicative that the neoplasia has potential for being treated by a cGMP-specific PDE inhibitor.

Claim 9. (withdrawn): The method of claim 8, wherein the method is carried out using a kit comprising an antibody that is immunoreactive with cGMP-specific PDEs and an immunodetection reagent.

Claim 10. (withdrawn): The method of claim 9, wherein the immunodetection reagent is selected from the group consisting of urease, alkaline phosphatase, (horseradish) hydrogen peroxidase, and glucose oxidase.

Claim 11. (withdrawn): The method of claim 8, wherein the method is carried out using a kit comprising:

- a) a first antibody, the first antibody being immobilized onto a solid phase, wherein the first antibody is immunoreactive with cGMP-specific PDEs;
- b) a second antibody, wherein the second antibody is immunoreactive with at least one member of the complex formed between the first antibody and cGMP-specific PDEs, and is linked to a detectable label;
- c) a washing buffer used to remove non-specifically bound immune complexes; and

d) reagents necessary for detecting the amount of detectable label.

Claim 12. (withdrawn): A method for identifying neoplasia from a patient responsive to treatment with a cGMP-specific PDE inhibitor comprising the steps of:

- a) obtaining a suspected neoplastic tissue sample from the patient;
 - b) exposing the suspected neoplastic tissue sample to a first antibody, the first antibody being immobilized onto a solid phase, wherein the first antibody is immunoreactive with cGMP-specific PDEs, under conditions effective to allow the formation of immune complexes;
 - c) washing the solid phase to remove non-specifically bound immune complexes;
 - d) exposing the solid phase to a second antibody, wherein the second antibody is immunoreactive with at least one member of the complex formed between the first antibody and cGMP-specific PDEs, and is linked to a detectable label;
 - e) washing the solid phase to remove non-specifically bound second antibody;
- and
- f) detecting the amount of detectable label to ascertain the level of cGMP-specific PDE protein,
- wherein an elevated amount of cGMP-specific PDE protein in the neoplastic tissue, relative to the amount in normal tissue, is indicative that the neoplasia has potential for being treated by a cGMP-specific inhibitor.

Claim 13. (withdrawn): A method for identifying neoplasias from a patient responsive to treatment with compounds that inhibit cGMP-specific PDEs comprising the steps of:

- a) obtaining a suspected neoplastic tissue sample from the patient;
- b) isolating nucleic acids from the suspected neoplastic tissue sample;
- c) contacting nucleic acids isolated from the tissue sample with an isolated cGMP-specific PDE nucleic acid segment under conditions effective to allow hybridization of substantially complementary nucleic acids; and
- d) detecting the hybridized complementary nucleic acids thus formed,

wherein an elevated amount of nucleic acid encoding for cGMP-specific PDEs in the neoplastic tissue, relative to normal tissue, is indicative that the neoplasia has potential for being treated by a cGMP-specific inhibitor.

Claim 14. (withdrawn): The method of claim 13, wherein the method is carried out using a kit comprising:

- a) reagents for isolating nucleic acids from a tissue sample; and
- b) an isolated cGMP-specific PDE nucleic acid segment.

Claim 15. (withdrawn): A method for identifying neoplasia from a patient responsive to treatment with compounds that inhibit cGMP-specific PDEs comprising the steps of:

- a) obtaining a suspected neoplastic tissue sample from the patient;
- b) isolating nucleic acids from the sample;
- c) contacting the nucleic acids isolated from the tissue sample with a pair of nucleic acid primers that hybridize to distant sequences of a cGMP-specific PDE, the primers being capable of amplifying a nucleic acid segment of a cGMP-specific PDE;
- d) conducting a polymerase chain reaction to create amplification products;
- e) detecting and characterizing the amplification products thus formed, whereby if the amplification products contain sequence coding for cGMP-specific PDEs, it is indicative that the neoplasia has potential for being treated by a cGMP-specific PDE inhibitor.

Claim 16. (withdrawn): The method of claim 15, wherein the method is carried out using a kit comprising:

- a) reagents for isolating nucleic acids from a tissue sample;
- b) a pair of nucleic acid primers that hybridize to distant sequences on a cGMP-specific PDE, the primers being capable of amplifying a nucleic acid segment of a cGMP-specific PDE; and
- c) reagents for conducting a polymerase chain reaction.

Claim 17. (new): A method for identifying neoplasias responsive to treatment with compounds that selectively inhibit neoplasia, comprising (a) removing a sample of neoplastic tissue from a patient, (b) growing cells from the sample as explants in vitro, (c) contacting a sample of said cells with a compound that has cGMP-specific PDE inhibition activity, (d) comparing the number of apoptotic cells in the presence of the compound with the number of apoptotic cells in the absence of the compound, and (e) determining whether the compound promotes an increase in apoptosis in the neoplasia.